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In Re Patent Application of:
Siani, M.A. *et al.*

Serial No.: 09/144,838

Filed: August 31, 1998

For: **Modular Protein Libraries and Methods of Preparation**

Examiner: Wessendorf, T.

Art Unit: 1627

Atty. Dkt.: 3504.183 GRFN 020/01-US

24 DS 8/7/01

Reply

Hon. Director of Patents
& Trademarks
Washington, D.C. 20231

Sir:

In Response to the Final Official Action of February 14, 2001, the time for responding to which has been extended by the accompanying Petition for an Extension of Time, Applicants respectfully submit the following amendments and remarks, and request reconsideration.

Amendments

In The Claims

Please cancel claims 1-27 and 37-51.

Please rewrite claims 28, 30, and 31-35 to read as follows:

28. **[Twice Amended]** A method of producing a cross-over protein that contains at least one peptide segment whose sequence is derived from a first protein and at least one peptide segment whose sequence is derived from a second protein, said method comprising:

ligating under chemoselective chemical ligation conditions (i) at least one N-

terminal peptide segment comprising a functional protein module derived from said first protein, and (ii) at least one C-terminal peptide segment comprising a functional protein module derived from said second protein having an amino acid sequence that is different from said first parent protein, wherein said N-terminal peptide segment and said C-terminal peptide segment comprise compatible reactive groups capable of chemoselective chemical ligation to one another, whereby a covalent bond is formed between said compatible reactive groups of said N-terminal peptide segment and said C-terminal peptide segment so as to produce a chemical ligation product comprising a cross-over protein having a C-terminus and an N-terminus.

30. **[Twice Amended]** The method of claim 28, wherein the first and second protein molecules from whose sequences said N-terminal peptide(s) and said C-terminal peptide(s) are derived belong to the same family of protein molecules.

31. **[Amended]** The method of claim 28, wherein said chemoselective chemical ligation is selected from the group consisting of native chemical ligation, oxime forming chemical ligation, thioester forming ligation, thioether forming ligation, hydrazone forming ligation, thiazolidine forming ligation, and oxazolidine forming ligation.

32. **[Twice Amended]** A method of producing a cross-over protein library whose members contain at least one peptide segment whose sequence is derived from a first protein and at least one peptide segment whose sequence is derived from a second protein, said method comprising:

ligating under chemoselective reaction conditions a plurality of unique N-terminal peptide segments each comprising one or more functional protein modules derived from said first protein and a plurality of unique C-terminal peptide segments each comprising one or more functional protein modules derived from a second protein having an amino acid sequence that is different from said first protein, wherein said N-terminal peptide

segments and said C-terminal peptide segments comprise compatible reactive groups capable of chemoselective chemical ligation to one another, whereby a covalent bond is formed between said compatible reactive groups of said N-terminal peptide segments and said C-terminal peptide segments so as to produce a plurality of chemical ligation products comprising a plurality of unique cross-over proteins each having a C-terminus and an N-terminus.

33. **[Amended]** The method of claim 32, wherein said plurality of N-terminal peptide segments are obtained by cross-over ligation of two or more different families of protein molecules.

34. **[Amended]** The method of claim 32, wherein said plurality of C-terminal peptide segments are obtained by cross-over ligation of two or more different families of protein molecules.

35. **[Twice Amended]** The method of claim 32, wherein the first and second protein molecules from whose sequences said N-terminal peptide(s) and said C-terminal peptide(s) are derived belong to the same family of protein molecules.